

## **IN THE DRAWINGS**

Please replace the original drawing sheet with the attached replacement drawing sheet of Fig. 1. The attached replacement drawing sheet deletes Fig. 1 and renumbers Figure 2 as Figure 1.

Attachment: Replacement Sheet

## REMARKS

Applicants hereby remove Figure 1 from the application, and have likewise removed reference to that Figure in the Description of the Drawings. Former Figure 2 is now amended to renumber that as Figure 1, and corresponding correction is likewise made to the Description of the Drawings. Applicants submit herewith a replacement drawing sheet for former Figure 2, now Figure 1.

In response to paragraph 3 of the Official Action, the specification is amended to label the legend appearing at the top of page 25 as being read with Table 3, i.e., A, B, C and D relate as follows: "Before coating (**A**)", "After coating (**B**)", "Lectin (**C**)" and "Microcapsulation (**D**)" in Table 3, respectively.. Applicants submit that this obviates the objection.

The objections as to claims 2 and 3 are mooted by the cancellation of those claims. The claims are canceled without prejudice or disclaimer.

The Section 112, first paragraph rejections as to claims 2 and 3 are likewise mooted by the cancellation of those claims.

The Section 112, second paragraph rejection of claim 1 is mooted by the instant amendments to the claim. The constituent elements of the claim are now recited more specifically.

The Section 112, second paragraph rejections of claims 2 & 3 are mooted by the cancellation of those claims.

The Section 112, second paragraph rejection of claims 1-3 is overcome by the instant amendments. Claim 1 has been amended to recite the various elements by reference to generic terms. The trademarks are not relied upon as descriptions of the goods themselves. Claims 2 -4 have been canceled, mooting those rejections.

**Prior Art Rejections**

*Thosar*

The claimed subject matter has been rejected as obvious over Thosar. Thosar does not teach or suggest the claimed invention. Thosar is non-analogous art.

As acknowledged in the rejection, Thosar is directed to alternative active agents. Moreover, Thosar is expressly directed to "Immediate Release Eplerenone Compositions." In contrast, the instant claims are directed to enteric coated formulations that avoid immediate release to prevent the active agent from being released in the more acidic contents of the stomach such that the formulation will pass through to the more basic intestinal tract, and be released there. Thus, one looking to formulate such a pharmaceutical composition would not have looked to Thosar for a solution to this particular problem.

Even if one were motivated to look to Thosar, there is no showing that such a worker would have arrived at the claimed invention. Rather, such a worker would have "optimized" the formulation to achieve a directly contrary result from aimed at by Thosar. There has been no showing about how one might have "optimized" the formulation, or how one would have optimized it, or what criteria one would have used to optimize it. If one had optimized the formulation for the same purpose as Thosar, then it would have been expected that such a worker would have arrived at a dramatically different formulation and combination of ingredients.

*Sauerbier & Cook*

Likewise, Sauerbier fails to teach or suggest the claimed invention. One skilled in the art seeking to make an enteric coated pharmaceutical formulation specifically designed to avoid gastric release of the active agent would not have looked to Sauerbier, and even if one were to have looked at Sauerbier, there has been no showing that the further manipulation of Sauerbier needed to arrive at the claimed invention would have produced the instantly claimed invention.

Sauerbier teaches compounding the active agent mesna into an effervescent tablet. One skilled in the art would have appreciated that the physicochemical requirements for an effervescent tablet are not the same as those for an enteric coated tablet for which one wishes to avoid release of an active agent in the stomach.

Further, the Sauerbier reference clearly states that the compounding of the pharmaceutical formulation disclosed in Sauerbier is dictated by the peculiar chemical properties and problems associated with the specific active ingredient, mesna. Col. 1, lines 34-57. Among those problems is the very unpleasant taste of the active agent, which significantly compromises patient compliance, particularly as the patient population is already likely to be suffering from loss of appetite and nausea. Additionally, mesna presents chemical challenges in formulation as the compound itself reacts with gelatin capsules, causing the capsules to split during storage. Col. 1, lines 45-50.

There has been no showing that the instant formulations suffer from those peculiar drawbacks, and so there has been no showing that one skilled in the art faced with making the enteric formulations of the instant claims would have either

resorted to the teachings of Sauerbier. And, and even if such worker were to resort to Sauerbier, there has been no showing that such worker would have arrived at the claimed invention.

The rejection acknowledges that Sauerbier does not disclose the use of zein in its pharmaceutical formulations, and asserts that Cook would have made such an addition obvious. However, there is no showing how or why one skilled in the art would have turned to Cook, nor is there any showing why one would have taken such a narrow teaching from Cook and applied it to the teaching of Sauerbier in the narrow and specific manner required to arrive at the claimed invention. Cook is likewise not directed to pharmaceutical formulations such as those of the instant claims. Indeed, Cook is not necessarily directed to pharmaceutical formulations, much less to specific enteric coated formulations designed to have specific dissolution properties. Rather, Cook is directed to the formation of shellac films, and particularly to shellac films that can be fabricated without the use of organic solvents, which demand special handling requirements. There has been no showing that one skilled in the art reading Cook would have applied those teachings to a problem analogous to that of Sauerbier, much less to that of the instant claims. Even if one were to have combined those references, there is no showing that one skilled in the art making that combination would have combined the various elements and teachings from the two references to arrive at the claimed invention. The asserted combination of Sauerbier and Cook is a classic hindsight reconstruction of the invention without any showing how or why the disparate elements from the two would have been combined to arrive at the claimed invention.

*Faour & Cook*

The combination of Faour and Cook likewise fails to teach or suggest the claimed invention. Faour relates to what is described as a "multi-layered osmotic device." The Faour device is designed to permit differential disposition of a first and second active agent. The device described is a complex structure having various elements for differential release of drugs in the device. Among other things, the device includes perforated passageways and a wall that is permeable to a fluid in the environment of use and substantially impermeable to the first active agent, and inert water soluble polymer coat comprising a PVP-vinyl acetate copolymer surrounding the semipermeable membrane and plugging the passageway in the wall, and an external coating having a second active agent for immediate release of the drug and wherein the first active agent is released from the core after the external coat has partially or completely dissolved or eroded. Although there are admittedly some of the same ingredients in the osmotic device of Faour, the Faour device is far more complicated, and has substantially different objectives, construction, and combinations of ingredients than that of the instant claims.

Cook is not directed to such an osmotic device, and there has been no showing that the teachings of Cook would have led one skilled in the art to devise the formulations of the instant claims. Even if one were to combine those non-analogous references and their widely disparate teachings, there is no showing that one would have combined them to arrive at the instant invention.

The rejection seems to suggest that the invention would have been derived out of mere optimization; however, the rejection fails to identify any teaching showing

what elements should be optimized, and for what purpose. In the absence of such a showing, there is no prima facie case of obviousness.

### **Conclusion**

In view of the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of all outstanding rejections. Applicants submit that the claims are now in condition for allowance, and respectfully request formal notification to that effect. If, however, the Examiner perceives any impediments to such a notice of allowability, whether substantive or formal, the Examiner is encouraged to call Applicants' attorney at the number provided below. Such informal communication will expedite examination and disposition of this case.

Respectfully submitted,

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